

some research has examined these variables in clinically-high-risk (CHR) groups, little research has examined nonclinical samples at risk for psychosis. Thus, this study sought to examine the relationship between ToM and neurocognition in a nonclinical sample with schizotypal traits, as research suggests these individuals may be at risk of developing a psychotic illness. It was hypothesized that lower performance in working memory and executive functioning would be related to poorer performance in cognitive and affective ToM, which would subsequently be associated with subsyndromal delusions. It was further predicted that schizotypal traits would moderate the relationship between neurocognitive performance and ToM abilities.

Methods: Undergraduate students (N = 99) completed self-report measures of personality and psychosocial functioning, including the Schizotypal Personality Questionnaire, Beck Depression Inventory-II, Launay-Slade Hallucination Scale-Revised, and 21-Item Peters Delusions Inventory. Participants also completed the Neuropsychological Assessment Battery Screening Module, which is a screening measure for neurocognitive dysfunction. Finally, they completed the Recognition of Faux Pas Test, a task-based measure that evaluates cognitive and affective ToM.

Results: Data collection is complete, and the data will be analysed using partial least squares structural equation modeling. This is a regression-based path analysis designed for exploratory models. This statistical method is better able to handle non-normally distributed data and smaller sample sizes when compared to covariance-based structural equation modeling.

Discussion: Study findings will be discussed in the context of cognitive models for the development of psychosis. The ways in which these findings, and cognitive models more broadly, can facilitate early detection of schizophrenia will be discussed, along with how such models can be used to inform psychosocial interventions for the illness.

S76. PROACTIVE AND REACTIVE RESPONSE INHIBITION IN INDIVIDUAL WITH SCHIZOTYPY: AN ERP STUDY

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Background: Schizotypy, a subclinical group at risk for schizophrenia, have been found to show impairments in response inhibition. Recent studies differentiated proactive inhibition (a preparatory process before the stimuli appears) and reactive inhibition (the inhibition of a pre-potent or already initiated response). However, it remains unclear whether both proactive and reactive inhibition are impaired in schizotypy and what are the neural mechanisms. The present event-related potential study used an adapted stop-signal task to examine the two inhibition processes and the underlying neural mechanisms in schizotypy compared to healthy controls (HC).

Methods: A total of 21 individuals with schizotypy and 25 matched HC participated in this study. To explore different degrees of proactive inhibition, we set three conditions: a “certain” go condition which no stop signal occurred, a “17% no go” condition in which stop signal would appear in 17% of trials, and a “33% no go” condition in which stop signal would appear in 33% of trials. All participants completed all the conditions, and EEG was recorded when participants completed the task.

Results: Behavioral results showed that in both schizotypy and HC, the reaction times (RT) of go trials were significantly prolonged as the no go percentage increased, and HC showed significantly longer go RT compared with schizotypy in both “17% no go” and “33% no go” conditions, suggesting greater proactive inhibition in HC. Stop signal reaction times (SSRTs) in “33% no go” condition was shorter than “17% no go” condition in both groups. Schizotypy showed significantly longer SSRTs in both “17% no go” and “33% no go” conditions than HC, indicating schizotypy relied more on reactive inhibition. ERP results showed that schizotypy showed larger overall N1 for go trials than HC irrespective of condition, which may indicate a compensation process in schizotypy. Schizotypy showed

smaller N2 on both successful and unsuccessful stop trials in “17% no go” conditions than HC, while no group difference was found in “33% no go” conditions for stop trials, which may indicate impaired error processing.

Discussion: These results suggested that schizotypy tended to be impaired in both proactive control and reactive control processes.

S77. ROLE OF DOPAMINE AND GLUTAMATE TRANSPORTERS IN GENERATION OF ANTIPSYCHOTIC EFFICACY

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Background: Antipsychotic drugs are the first line intervention to treat psychosis in schizophrenia and D2 receptor blockade is thought to be their primary mechanism of action. However, multiple lines of evidence from human and animal studies show that D2 receptor blockade is not always correlated with markers of antipsychotic efficacy. We previously demonstrated that reduced antipsychotic efficacy occurs after chronic antipsychotic administration in rodents despite stable D2 blockade, examined using PET imaging. Instead, we found that changes in expression of the dopamine transporter (DAT) were associated with decreases in endogenous dopamine and dopamine-mediated autoinhibition. These studies have led us to examine the DAT as a critical player in generation of an antipsychotic response.

Methods: Using antisense morpholino oligonucleotides, administered for 3 consecutive days using Long Evans rats, we selectively blocked translation of DAT or GLT-1 mRNA in the core of the nucleus accumbens, a brain region critical for motor outputs in response to salient stimuli. Baseline locomotion was monitored prior to and after an acute i.p. injection of haloperidol. Next, locomotion was monitored in response to a tail pinch or acute i.p. administration of cocaine. Transporter expression was quantified during acute or chronic haloperidol treatment using confocal microscopy.

Results: We found that DAT knockdown enhanced tail pinch-induced locomotion after acute haloperidol administration. Additionally, knockdown of the glutamate transporter GLT-1 strongly enhanced locomotion induced by tail pinch or cocaine injection after antipsychotic treatment. Confocal analysis of GLT-1 expression after acute or chronic haloperidol revealed significant GLT-1 up-regulation during a time period associated with antipsychotic efficacy.

Discussion: Our findings demonstrate a cause/effect relationship between reduced DAT and the behavioral response to an acute injection of antipsychotics in rodents. In all, our data point to the importance of both dopamine and glutamate uptake in the efficacy of antipsychotic drugs and argue against a D2-centric hypothesis of antipsychotic action.

S78. TIME PREDICTION AND SENSE OF SELF: LACK OF FLEXIBILITY IN PATIENTS WITH SCHIZOPHRENIA

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Background: The sense of time continuity appears to be disturbed in pathologies like schizophrenia, associated with a disruption of the sense of self, and of the feeling of being immersed in the world. Prediction mechanisms have been proposed to be involved in the sense of time continuity by helping to relate discontinuous events, and our previous studies have suggested that these mechanisms may occur even at the millisecond level. Such mechanisms would be involved in our ability to interact with the outer world, by helping to follow events accurately in both space and time. We explored prediction mechanisms and attention shifts based on recently experienced sequences of visual information (sequential effects).

Methods: 26 patients with schizophrenia and 20 matched controls were included in asynchrony discrimination tasks, and assessments of minimal self disorders with the EASE. On each trial, two stimuli are displayed with varying stimulus onset asynchronies (SOA). Subjects decide whether the stimuli are simultaneous or asynchronous and give manual responses. Sequential effects were explored further in several groups of 15 healthy participants.

Results: The main finding in controls is a strong accuracy advantage for different- as compared to same-order trials, but only when trial t is with an SOA slightly larger than trial $t-1$ (advantage of 16% in accuracy), or equivalent (advantage of 10% in accuracy). An advantage for same-vs. different-order trials is observed only when the SOA on the previous trial is large and visible. In patients, there is no advantage for same-order trials. There is a clear advantage for different-order trials (advantage of 16% in accuracy), but this effect disappears, contrary to controls, when SOAs are equivalent on successive trials (1% difference in accuracy). The impairment in the trial-to-trial effects in patients correlates with minimal self disorders (the EASE).

Discussion: Further investigations in healthy participants suggest that the sequential effects can be explained in terms of prediction of stimulus sequences from trial to trial, which are accompanied by an attention shift. The first stimulus triggers the onset of the sequence, and attention is then covertly shifted in space and time according to the previous trial, in order to attend to the second stimulus. This explains the advantage for different-order trials: when order is reversed on the present trial, attention ends up in the location of the first stimulus of the present sequence. This first stimulus is perceived as isolated on the screen if the second stimulus occurs later than on the previous trial, thus facilitating the detection of an asynchrony. The asynchrony is then obvious, explaining the large amplitude of the effect. The fact that the effect extends to the condition in which SOAs are equivalent on successive trials suggests that participants shift their attention in advance, as if anticipating the location of the second stimulus. This is impaired in patients, who replay sequences of events, but do not anticipate the successive events flexibly. This would impair their immersion in the world, where events rarely happen twice at the same time exactly.

S79. REINFORCEMENT LEARNING ABNORMALITIES IN INDIVIDUALS AT CLINICAL HIGH RISK AND IN THE FIRST EPISODE OF PSYCHOSIS

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Background: Prior studies indicate that chronic schizophrenia (SZ) is associated with a specific profile of reinforcement learning abnormalities. These impairments are characterized by: 1) reductions in learning rate, and 2) impaired Go learning and intact NoGo learning. Furthermore, each of these deficits are associated with greater severity of negative symptoms, consistent with theoretical perspectives positing that avolition and anhedonia are associated with deficits in generating, updating, and maintaining mental representations of reward value that are needed to guide decision-making. However, it is unclear whether these deficits extend to earlier phases of psychotic illness and when individuals are unmedicated.

Methods: Two studies were conducted to examine reinforcement learning deficits in earlier phases of psychosis. In study 1, participants included 35 participants with first episode psychosis (FEP) and 25 healthy controls (HC). Study 2 included 17 antipsychotic naïve individuals who met criteria for attenuated psychosis syndrome (APS) (i.e., those with a prodromal syndrome) and 18 matched healthy controls (HC). In both studies, participants completed the Temporal Utility Integration Task, a measure of probabilistic reinforcement learning that contained Go and NoGo learning blocks.

Participants in the clinical groups also completed neuropsychological testing and standard clinical interviews designed to determine symptom severity and diagnosis.

Results: FEP displayed impaired Go learning and intact NoGo learning. In contrast, APS did not display impairments in Go or NoGo learning at the group level. Negative symptoms were not significantly associated with reinforcement learning in APS participants. However, greater impairments in Go learning were associated with increased cross-sectional risk for conversion on the NAPLS risk calculator score in the APS group.

Discussion: Findings provide new evidence for areas of spared and impaired reinforcement learning in early phases of psychosis. Similar to chronic SZ, FEP was associated with impaired Go learning, and intact NoGo learning. Reinforcement learning is more spared in those at clinical high-risk, except those at greatest risk for conversion, where Go learning deficits are more pronounced. These findings suggest that reinforcement learning deficits may emerge early among those who are at clinical high risk for developing psychosis and that they are already pronounced by illness onset in the first episode. Importantly, these reinforcement learning deficits do not appear to be a byproduct of illness chronicity or antipsychotic medication use, but rather a consequence of the illness itself.

S80. CHILDHOOD TRAUMA AND SOCIAL COGNITION IN DELUSIONAL PSYCHOSES

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Background: Deficits in social cognition could be involved in the pathogenesis of delusions in psychotic disorders (Bentall et al., 2009). Childhood trauma (CT) has been associated with an increased risk for psychosis (Varese et al., 2012). Neurocognitive and social cognition deficits could mediate in the association between CT and psychosis (Mansueto et al., 2019). Social cognition and childhood trauma have been understudied so far in delusional disorder (DD). We aimed to assess social cognition in a sample of patients with delusional psychoses (i.e., DD and schizophrenia) and healthy controls (HC) and to explore the potential effect of childhood trauma on social cognition and delusion.

Methods: This cross-sectional, transdiagnostic study included 69 patients with a DSM-IV-TR-confirmed diagnosis of DD (mean age 44.06 ± 11.39 years, 53.6% female), 77 with DSM-IV-TR-confirmed schizophrenia (mean age 38.12 ± 9.27 years, 27.3% female), and 63 HC (mean age 43.6 ± 13.0 years, 68.3% female). Attributional bias was assessed with the "Internal, Personal, and Situational Attributions Questionnaire." Theory of Mind (ToM) performance was assessed with the "Reading the Mind in the Eyes Test" and the "Faux Pas Recognition Test." Childhood trauma was measured with the "Childhood Trauma Questionnaire." Neuropsychological functioning was measured with a comprehensive battery assessing attention, verbal learning, working memory, and executive function. We used ANCOVAs and linear regression analyses to assess the association between the three measures of social cognition and i) diagnosis, ii) dimensional measures of delusion proneness (Peters Delusion Inventory, PDI) and intensity (Maudsley Assessment of Delusion Schedule, MADS), and iii) childhood trauma; after controlling for potential confounders (age, sex, socioeconomic status, and estimated premorbid intelligence quotient).

Results: Patients with DD showed significantly poorer performance on the "Eyes Test" than HC (Cohen's $d = -0.44$, $p = 0.037$), after controlling for potential confounding variables. The difference was no longer significant